

EXHIBIT A

Pat. No.	Initials	Date of birth	Diagnosis	Date commenced treatment	Concentration of Aloderm	Concomitant treatment	Notes
1	RJ	26/5/89	Atopic dermatitis since 18 months old	December 1997	7.5% and 4% lotions	Hydrocortisone 1%	7.5% effective and well tolerated. Eczema improved. Itching recommenced 2 days after stopping Aloderm. 4/3/98. Transferred to Aloderm. Eczema well controlled, reduced use of hydrocortisone. 25/1/98: Had flare up of eczema. Aloderm caused stinging sensation treated with hydrocortisone. Aloderm OK again after one day. Treatment stopped early 1999 as skin clear.
2	JK	3/8/95	Atopic dermatitis soon after birth	December 1997	5% foam 7.5% lotion	Unguent Metic 1% Hydrocortisone Calmurid cream x 2 daily	Neither 5% foam nor 7.5% lotion well tolerated. Both resulted in the sensation. Aloderm stopped.
3	JL	13/5/85	Eczema since 6 months old.	June 1998	4% lotion	Aureocort when had otherwise Eumovate.	Eczema affects hands. Improved after starting Aloderm 4%. Continued use with benefit.
4	TR	3/3/95	Atopic eczema since 3-4 weeks old	September 1998	4% lotion		2/9/98: Skin considerably better after using Aloderm for one week. 20/9/98: Started cold and had flare up of eczema. Skin very red and Aloderm caused hot feeling. Stopped and used Aureocort. Skin settled and after 24 hours was able to use Aloderm without problems. Continued to use Aloderm with benefit.
5	JK	22/5/94	Atopic eczema since 21 months old.	November 1998	4% lotion	Wet wrapping and Eumovate	8/12/98: Skin initially improved after starting Aloderm. Then developed severe asthma attack (needed oral steroids). Aloderm started to cause sensation so was stopped. Not tried again.
6	ALK	6/12/91	Eczema since 5 weeks old	December 1997	7.5% lotion 5% foam	Eumovate	Initial improvement but 7.5% lotion later caused stinging. Transferred to 5% foam without problems. Treatment stopped as no longer required.
6	MJC	25/9/74	Atopic eczema since childhood	December 1998	4% lotion	Hydrocortisone 1%	30/12/98: Eczema mainly on arms, neck, thighs.
7	JA	20/8/49	Eczema since teenager	February 1999	4% lotion	Steroid creams	7/1/99: Skin improved. Subsequently lost to follow up.
8	AJB	24/5/97	Eczema since 2-3 weeks old	November 1999	2% lotion	Hydrocortisone	Made itching worse for first few days. Then skin improved. By April skin normal on Aloderm alone. Not needing steroids. Last contact Jan 2003 - still OK.
9	PK	3/1/67	Mild eczema	November 1999	2% lotion	None	Skin improved. Aloderm well tolerated. Left for Australia Dec 1999. Eczema cleared in Australia. No further treatment required.
10	APT	26/4/95	Eczema since 6 weeks	May 1999	4% lotion	Steroids	No benefits from Aloderm. Discontinued.
11	BJW	5/10/95	Eczema since 8 weeks	February 1999	4% lotion	Steroids Wet-wrapping	Skin improved. Aloderm caused hot sensation during flare up. OK restarted after flare-up treated with steroids. No contact since June.
12	DW	31/5/82	Hand dermatitis Due to shampoos	March 2000	4% lotion	None	Dermatitis improved. Has had 2 flare ups needing additional steroid otherwise controlled on Aloderm alone. Continues as trainee hairdresser.
13	FB	14/7/83	Eczema	September 2000	4% lotion	Steroids	Last contact July 2001 - still OK with Aloderm.
Pat.	Initials	Date of birth	Diagnosis	Date	Concentration	Concomitant	Notes

No.	birth		commenced treatment	of Alloderm	treatment		
14	CS	2/10/56	Facial eczema	August 2002	4% lotion	None	Improved. Last seen 30/01/03
15	AM	15/4/89	Atopic dermatitis	September 2001	4% lotion	Steroids	Improved but sometimes noticed heat effect. Heat effect not a problem during exacerbations. Last seen January 2003. Still has benefit.
16	CS	5/9/98	Atopic dermatitis	June 2002	4% lotion	None	Overall benefit in skin condition. Last seen February 2003. Treatment continuing.
17.	WA	25/5/63	Severe dermatitis	Sept 2002	4 % Lotion	None	Of no benefit. Had heat sensation. Treatment stopped. Total IgE 241
18	MH	27/11/85	Mild facial eczema	Feb 2002	4%lotion	None	Of some benefit. Treatment stopped September 2002 as no longer required. Treatment restarted March 2003 and benefit resumed.
19	ADB	15/9/52	Contact dermatitis	Jan 2002	4%lotion	None	Of some benefit but found lotion had drying effect. Treatment continued (1/6/03)
20	BR	20/12/95	Eczema	Jan 2002	4% lotion	None	Heat sensation treatment stopped.
21	JV	Aged 31	Dermatitis	May 2003	4% lotion	None	Mild dermatitis only. Itched at first then better. 5/6/03 still on treatment with benefit.
22	LH	11/7/95	Atopic dermatitis	31/1/02	4% lotion		Doing well on Alloderm. Last seen 1/5/03
23	SS	30/4/63	Atopic dermatitis	1/5/03	4% lotion	None	Better on Alloderm alone
24	EW	7/10/99	Atopic dermatitis	20/2/03	4% lotion	Steroids	Helped by Alloderm.
25	EC	16/6/63	Eczema	October 2002	4% lotion	None	Helped by Alloderm
21	RH	23/10/99	Eczema	May 2002	4% lotion	Hydrocortisone	Helped by Alloderm. Only need to use hydrocortisone occasionally
22	TW	03/05/98	Atopic dermatitis	November 2002	4% lotion	Eumovate	Helped by Alloderm. Last contact May 2003
23.	AW	6/4/93	Atopic dermatitis	January 2003	4% lotion	None	Helped
24.	OB	06/02/00	Atopic dermatitis	October 2002	4% lotion	Hydrocortisone	Helped. Last contact June 2003
25	LB	06/02/00	Atopic dermatitis	October 2002	4% lotion	Hydrocortisone	Helped. Last contact June 2003. Only used hydrocortisone occasionally
26.	IP	26/09/97	Atopic dermatitis	October 2002	4% lotion	None	Helped by Alloderm. Very occasional use of steroid. 1 day in 7
27.	CD-B	23/02/95	Atopic dermatitis	November 2002	4% Lotion	None	Helped by Alloderm. Last contact May 2003
28.	LW	03/08/96	Atopic dermatitis	November 2002	4% lotion	None	Helped by Alloderm. Last contact March 2003
29	SW	02/05/93	Atopic dermatitis	November 2002	4% Lotion	None	Helped by Alloderm. Last contact March 2003
30	MP	15/07/93	Atopic dermatitis	November 2002	4% lotion	Fuebet (steroid)	Helped by Alloderm. Last contact February 2002
31	CG	04/07/91	Atopic dermatitis	November 2002	4% lotion	Fucidin (antibiotic)	Helped by Alloderm. No steroids used. Last contact February 2002
32	ZF	12/12/98	Atopic dermatitis	October 2002	4% lotion	None	Helped by Alloderm. Very occasional use of steroid cream off exacerbation. Last contact June 2003
33.	GC	27/09/92	Atopic dermatitis	November 2002	4% lotion	Hydrocortisone	Helped. Last contact April 2002
34	JF	10/09/98	Atopic dermatitis	December 2002	4% lotion	Haelen (steroid cream)	Helped. Last contact March 2003
35	KK	3 years	Atopic dermatitis	September 2002	4% Lotion	None	Helped. Last contact February 2003
36	CH	20/03/00	Atopic dermatitis	November 2002	4% lotion	Hydrocortisone 1%	Helped by Alloderm. Last contact March 2003
37.	JH	07/12/98	Atopic dermatitis	November 2002	4% lotion	Hydrocortisone 1%	Helped by Alloderm. Last contact March 2003
38.	DK	22/10/96	Atopic dermatitis	November 2002	4% lotion	Hydrocortisone 1%	Helped by Alloderm. Last contact March 2003
39	GR	4 years	Atopic dermatitis	March 2002	4% lotion	Emollients	Alloderm caused stinging and redness - stopped.
40	HS	19/11/95	Atopic dermatitis	December 2002	4% Lotion	None	Helped by Alloderm. Last contact June 2003

FROM HAUGEN LAW FIRM PLLP

(MON) 9/29/03 11:16/ST. 11:07/NO. 4862017331 P 27

EXHIBIT B

Eur J Pediatr (1989) 149: 74

European Journal of

Pediatrics

© Springer-Verlag 1989

Letter to the editors

Nedocromil sodium cream
in the treatment of atopic dermatitis

H.P. Van Bever and W.J. Stevens

Departments of Paediatrics and Immunology,
University Hospital Antwerp, B-2320 Antwerp, Belgium

Sir: There have been a number of studies on the effect of topical sodium cromoglycate in atopic dermatitis. In most of these studies topical sodium cromoglycate failed to show any significant activity [2, 4].

Recently, nedocromil sodium was developed. This drug showed activity similar to that of sodium cromoglycate but is markedly more potent [1].

Since mast cell involvement has been observed at some stage in the development of various skin disease including atopic dermatitis [3], nedocromil sodium seems to be an obvious candidate for investigation in the area of atopic dermatitis.

Therefore, we undertook a double-blind, parallel group trial in which following a 2-week baseline period, atopic dermatitis patients were assigned randomly to either a 4% nedocromil sodium cream or a placebo for 4 weeks. The cream (nedocromil sodium or placebo) was applied twice daily. For dermal application, nedocromil sodium was formulated as an oil-in-water cream, stabilised with glyceryl monostearate and cetostearyl alcohol. It was maintained at pH 5.6 (= skin surface pH) by a sodium acid citrate/sodium hydroxide buffer, and preserved using a combination of parabens and potassium sorbate. In skin permeation tests using hairless mouse skin in vitro, a penetration rate of $2\mu\text{g}/\text{cm}^2$ per hour of nedocromil sodium, was observed. As placebo, the same cream was used but without nedocromil sodium. Both preparations were kindly supplied by Fisons Pharmaceuticals, Loughborough, England.

Twenty-six patients with atopic dermatitis (13/26 patients were between the age 12-16 years) entered the trial of whom 2 dropped out during the baseline period.

The 2 treatment groups (2 x 12 patients) were similar according to; sex, age (mean: 16 years, range: 12-47 years), weight, duration of atopic dermatitis, severity of atopic dermatitis during the last 12 months, present severity at the start of the trial and co-existence of bronchial asthma.

Evaluation of the treatment was performed using:

1. A daily score card for severity of atopic dermatitis was completed using a four-point score for day itching, night itching, sleep and overall severity of the skin lesions. For each treatment mean scores were computed for the baseline

period, weeks 1 and 2 of the treatment and weeks 3 and 4 of the treatment. The differences of the final period from the baseline for the two treatments were compared by the Mann Whitney U-test.

2. Clinical examination every 2 weeks during the trial, using a physician's five-point score for the severity of skin lesions.

3. The frequency of the use of an "escape" treatment (a 1% hydrocortisone containing cream).

Results

During the treatment phase, nine patients were withdrawn. Six (four on placebo) of these due to a gradual deterioration of the atopic dermatitis. Two (one on each treatment) due to a rapid deterioration, and one on nedocromil sodium because of a suspected adverse reaction (increased dryness of the skin).

By the use of the daily symptom score, no significant difference could be detected between the two treatments (Mann-Whitney U-test).

After 4 weeks treatment both patients and clinician could not detect any difference between the two treatments using a five-point score. The two groups showed also the same usage of the escape treatment.

Seventeen episodes of flaring of symptoms were recorded during the active treatment period, 9 of these were in the patients treated with nedocromil sodium. One caused withdrawal from the trial because of dryness of the skin in a patient treated with nedocromil sodium and one caused treatment to be stopped for 6 days because of furunculosis. This was observed in a patient treated with placebo. However, the most common symptoms were exacerbations of atopic dermatitis and itching.

In conclusion, 4% nedocromil sodium cream, applied during 4 weeks, twice daily has no advantage over placebo in the treatment of patients (older children and adults) with atopic dermatitis. No data are yet available on the use of nedocromil sodium cream in young children with atopic dermatitis.

References

1. Eady RP (1986) The pharmacology of nedocromil sodium. *Eur J Respir Dis [Suppl]* 69: 112-119
2. Haider SA (1977) Treatment of atopic eczema in children: clinical trial of 10% sodium cromoglycate ointment. *Br Med J*: 1570-1572
3. Hanifin JM (1984) Atopic dermatitis. *J Allergy Clin Immunol* 73: 211-222
4. Thimmothy T, Greaves MW (1978) Disodium cromoglycate ointment in atopic eczema. *Br Med J*: 500-501

Received March 15, 1989 / Accepted May 25, 1989